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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,722	11/28/2000	John P. Anderson	00228-US-NEW2C1	9856

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EXAMINER
WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/29/2003

5465

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/723,722	ANDERSON ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,18-20,22-25,27-37 and 39-131* is/are pending in the application.

4a) Of the above claim(s) *5-13,37 and 39-131* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,18-20,22-25 and 27-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: sequence alignments, publications used in 102 and 103 rejections..

The Response to Restriction Requirement filed on Jan. 2, 2003 as paper No. 13, and Supplemental Response to Restriction Requirement and Amendment filed on Feb. 14, 2003, as paper No. 17, are acknowledged. The Amendments to the claims and specification have been entered as requested. Claims 14-17, 26 and 32 are canceled. Claims 1-13, 18-20, 22-25, 27-37, and 39-131 are pending in the application. Claims 1-4, 18-20, 22-25, 27-36 are the subject of this Office Action.

DETAILED ACTION

1. Restriction/election

Applicant's election, with traverse, of Group I, claims 1-22 and 37-53 is acknowledged. The previous examiner found arguments of the Applicants persuasive and during the interview on January 27, 2003, agreed to rejoin Group I, II and III. Thus, the new Group I comprises claims 1-53, directed to beta-secretase protein. This restriction is proper and made final.

During the same interview on January 27, 2003, the previous examiner required the election of species. In response to this requirement Applicants elected the polypeptide of SEQ ID NO: 43. The claims readable on the elected species are 1-4, 18-20, 22-25, and 27-36. The claims are the subject of examination on merit. Claims 5-13, 21, 37, 39-53 are withdrawn from consideration as drawn to the non-elected species, see 37 CFR 1.142(b),

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

2. Objections

2.1. Specification

Description of Fig. 5 on page 8 is objected to, because it is confusing about the term proenzyme. The description states that SEQ ID NO: 43 is "the proenzyme region corresponding to amino acids 46-501", whereas in the same description Applicant write that the putative pro- region consists of residues 22-45; SEQ ID NO: 47. Thus residues 46-501 represent the mature enzyme and not proenzyme. Please correct the description of Fig. 5.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

2.2. Claims

Claims 1, 23 and 27 are objected to for the improper quotation of the amino acid residues, e.g., [46—501]. The correct quotation is "amino acid residues 46-501 of SEQ ID NO: 2."

3. Rejections

3.1. 35 USC, section.112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

The claims 18, 19 and 27-36 are rejected because they do not further limit the base claims 1 and 23 from which they depend. It seems that the scope of the claims is broader than that of the base claims 1 and 23.

SEQ ID NO: 43 consist of 456 amino acids. Claim 18 recites the polypeptide consisting of residues 63-501 of SEQ ID NO: 2, which is 438 amino acids; this polypeptide is in 96% identical to SEQ ID NO: 43. However, the claim also recites the polypeptides consisting of amino acid residues 63-452 of SEQ ID NO: 2, which consists of 390 amino acids, i.e., it is only 85% identical to SEQ ID NO: 43.

Claim 27 recites the polypeptide consisting of residues 63-501 of SEQ ID NO: 2, which is 438 amino acids; this polypeptide is in 96% identical to SEQ ID NO: 43. However, the claim also recites the polypeptides consisting of amino acid residues 58-452 of SEQ ID NO: 2, which consists of 395 amino acids, i.e., it is only 87% identical to SEQ ID NO: 43.

Claims 28-36 are rejected as depending on claim 27, because they do not correct deficiencies of the claim from which they depend.

3.2. 35 USC, section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

1. A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1–4, 18-19 and 22 are rejected under 35 U.S.C. 102(g) as being anticipated by US patent No. 6,319,689, issued to Powell et al. on Nov. 20, 2001, with priority date Jan. 28, 1997.

The claims are directed to a beta-secretase enzyme protein purified to apparent homogeneity comprising a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43.

Powell discloses the full amino acid sequence, i.e., 501 amino acids, of human beta-secretase identical to SEQ ID NO: 2 in the instant application. In the patent he sequence is also identified by SEQ ID NO: 2. SEQ ID NO: 2 comprises a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43; see the enclosed sequence alignment.

2. A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the

requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 20 is rejected under 35 U.S.C. 102(g) as being anticipated by US patent No. 6, 420, 534, issued to Gurney et al. on July 16, 2002, with priority date September 24, 1998.

The claim is directed to a beta-secretase from mouse purified to apparent homogeneity comprising a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43.

Gurney discloses the full amino acid sequence, i.e., 501 amino acids, of mouse beta-secretase identified by SEQ ID NO: 8. SEQ ID NO: 43 are in 98.8% identical to Gurney's SEQ ID NO: 8.

Thus, SEQ ID NO: 8 of the patent, the full length mouse beta secretase comprises a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43, see the enclosed sequence alignment.

3.3. 35 USC section.103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-25, 27-36 and are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,319,689, issued to Powell et al on Nov. 20, 2001, with priority date Jan. 28, 1997, in view of the common knowledge in molecular biology.

Claims 23-25 and 27-30 are directed to a composition of a β-secretase wherein

(1) Said beta-secretase is purified to apparent homogeneity,

(2) said beta-secretase is non-glycosylated or glycosylated,

(3) and form wherein the said beta-secretase comprises a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43, and wherein

(4) said beta-secretase is in crystalline form with or without an inhibitor.

Regarding point (1), the fact that β-secretase is purified to the apparent

homogeneity is not a characteristic feature of the enzyme as such, unless the inventors disclose a new method specifically directed to purification of β-secretase, this, however, is not the case.

With respect to point (2) the fact that β-secretase is in its glycosylated or non glycosylated form is not a characteristic feature of the enzyme as such, unless the inventors disclose a new method specifically directed to glycosylation or deglycosylation of the protein, this, however, is not the case. The protein in both forms is produced in the cell expressing the beta-secretase gene.

Regarding point (3), Powell does disclose human beta-secretase having SEQ ID NO: 2 in the patent. This beta-secretase comprises a peptide that is fewer than 460 amino acids in length, and includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 43. Powell also teaches composition comprising said beta-secretase protein; see column 19, line 13 and 46.

Powell, however does not disclose the composition of beta-secretase, or said beta-secretase with an inhibitor, wherein the protein is in crystalline form.

It would have been obvious to one having ordinary skill in the art at the time of invention to have the composition of beta secretase taught by Powell and modify it by crystallization of the enzyme.

The motivation that is obvious to one having ordinary skill in the art is to have the composition that is in more stable form than dissolved protein and the composition that enables crystallographic studies of interaction between the enzyme and its inhibitor with the purpose of improving the inhibitor properties. The other motivation is provided by

Powell et al. who write in column 19, line 28: "This invention provides methods of treating abnormal conditions...related both an excess and insufficient amounts of ASP2 polypeptide activity [beta-secretase, M.W.]. If the activity of ASP2 polypeptide is in excess, several approaches are possible." In line 46, Powell et al. write, "In another approach, soluble forms of ASP2 polypeptides still capable of binding the ligand in competition with endogenous ASP2 polypeptide may be administered." Crystalline solution of the beta-secretase is more stable than soluble form of that protein and when administered to a subject in need is converted in the body in a soluble form.

The probability of success in obtaining the claimed invention is 100%, because the methods of protein crystallization are routinely used in the art.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was, as a whole, *prima facie* obvious.

3. 4. Provisional double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that the applications Serial Nos. 09/471,699; 09/724,571; 09/501, 708; 09/ 723-739; 09/724,566; 09/724-568; 09/724,569 of the same inventive entity disclose polypeptide of SEQ ID NO:43, which is elected by Applicants. Said applications disclose also other truncated forms of beta-secretase enzyme set forth by SEQ ID NO: 2 in the instant application. Applications Serial Nos. 09/471,699; 09/724,571; 09/501, 708; 09/ 723-739; 09/724,566; 09/724-568; 09/724,569 also disclose compositions comprising polypeptides in crystalline form with or without inhibitors. Not all of these applications are available to the examiner at this time. If, upon availability of the above applications to the examiner, it is determined that there are conflicting claims between application Serial Nos. 09/471,699, 09/724,571, 09/501, 708, 09/ 723-739, 09/724,566, 09/724-568, 09/724,569 and the instant application, double patenting will not be considered as new ground(s) of rejection.

4. Conclusion

All claims are rejected. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Patent Examiner

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